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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/049,868	06/04/2002	Hans Deckmyn	522-1778	2345

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CLARK & ELBING LLP
101 FEDERAL STREET
BOSTON, MA 02110

EXAMINER	
HADDAD, MAHER M	

ART UNIT	PAPER NUMBER
1644	

DATE MAILED: 09/13/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/049,868	DECKMYN ET AL.	
	Examiner	Art Unit	
	Maher M. Haddad	1644	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *29 June 2006*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *65,66,70,71 and 80-82* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☒ Claim(s) *80-82* is/are allowed.

6)☒ Claim(s) *65 and 66* is/are rejected.

7)☒ Claim(s) *70 and 71* is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

1. Claims 65-66, 70-71 and 80-82 are pending.

Response to Arguments

2. In view of the Appeal Brief filed on June 29, 2006, PROSECUTION IS HEREBY REOPENED. New grounds of rejection are set forth below.

To avoid abandonment of the application, appellant must exercise one of the following two options:

(1) file a reply under 37 CFR 1.111 (if this Office action is non-final) or a reply under 37 CFR 1.113 (if this Office action is final); or,

(2) request reinstatement of the appeal.
If reinstatement of the appeal is requested, such request must be accompanied by a supplemental appeal brief, but no new amendments, affidavits (37 CFR 1.130, 1.131 or 1.132) or other evidence are permitted. See 37 CFR 1.193(b)(2).

3. In view of the new grounds of rejection presented below, the present Office Action is made NON-FINAL. Applicant's arguments made in the Appeal Brief will be addressed as they pertain to the new ground of rejection.

4. The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

5. Claims 65-66 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a pharmaceutical composition comprising the monovalent antibody fragment obtained from the monoclonal anti body produced by the cell line deposited with LMBP 5108CB or the variable region of a monovalent antibody fragment comprises SEQ ID NO: 4 and a pharmaceutical acceptable carrier, does not reasonably provide **enablement** for a pharmaceutical composition comprising any monovalent antibody fragment with binds in vivo to human platelet glycoprotein GPIb without incurring thrombocytopenia in claim 65, wherein the fragmen is a Fab fragment or a single variable domain. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and or use the invention commensurate in scope with this claim.

The specification disclosure does not enable one skilled in the art to practice the invention without an undue amount of experimentation.

In view of applicant's admission on page 14 of the brief dated 6/29/06 that Bergmeir teaches that antibody binding to GPIb resulted in thrombocytopenia, regardless of whether the antibody is a F(ab)2, Fab or scFv, therefore, it cannot be seen how any monovalent antibody fragment including Fab or single variable domain can be used in a pharmaceutical composition in vivo since they cause thrombocytopenia. Further, evidenced by Asch et al that a GPIb alpha specific 3G6 monoclonal antibody did not inhibit restocein-induced platelet aggregation (see page 1600, under antibodies in particular). A fragment of 3G6 monoclonal antibody including Fab and a single variable domain would not be expected to inhibit ristocetin-induced platelet aggregation and hence un-functional monovalent antibody fragments.

Reasonable correlation must exist between the scope of the claims and scope of the enablement set forth. In view on the quantity of experimentation necessary the limited working examples, the nature of the invention, the state of the prior art, the unpredictability of the art and the breadth of the claims, it would take undue trials and errors to practice the claimed invention.

6. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless --

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

7. Claims 65-66 are rejected under 35 U.S.C. 102(b) as being anticipated by Tandon et al (Biochem. J. (1991) 274:435-542).

Tandon et al reference teaches anti-glycocalicin Fab fragments against GPIb in 40 μg/well (page 537 under Role of membrane glycoproteins in particular). Further, Tandon et al teach that the platelets that were added to the well were in buffer A in the adhesion assay (see page 536, under Microtitre adhesion assay in particular), wherein buffer A is 5.0 mM-Tris, 5.5 mM-glucose, 150 mM-NaCl, 2.0 mM-MgCl2 and 0.5% BSA, pH 7.4. Buffer A is considered to be a pharmaceutical acceptable carrier. It is noted that glycocalicin is a proteolytic product of GPIbα.

While the prior art teachings may be silent as to the "binds in vivo to human platelet glycoprotein GPIb without incurring thrombocytopenia" per se; the product used in the reference is the same as the claimed product. Therefore, the claimed "binds in vivo to human platelet glycoprotein GPIb without incurring thrombocytopenia" is considered inherent properties.

The Tandon et al reference teaches the same products and the intended uses do not carry patentable weight per se and the claims read on the active or essential ingredients of the Fab fragment against GPIb.

When a claim recites using an old composition or structure (e.g. Fab fragments against GPIb antibody) and the use is directed to a result or property of that composition or structure (binds in

vivo to human platelet glycoprotein GPIb without incurring thrombocytopenia), then the claim is anticipated. See MPEP 2112.02. Also, see Bristol-Myers Squibb Co. v. Ben Venue Laboratories, Inc. 58 USPQ2d 1508 (CA FC 2001); Ex parte Novitski 26 USPQ 1389 (BPAI 1993); Mehl/Biophile International Corp. V. Milgraum, 52 USPQ2d 1303 (Fed. Cir. 1999); Atlas Powder Co. V. IRECO, 51 USPQ2d 1943 (Fed. Cir. 1999).

The reference teachings anticipate the claimed invention.

8. Claims 65-66 are rejected under 35 U.S.C. 102(b) as being anticipated by Wicki et al (Eur J Biochem. 1985 Nov 15;153(1):1-11).

Wicki et al teach treatment of washed platelets with Fab fragments of rabbit antibodies to the 45-kDa fragment of glycocalicin (a major proteolytic cleavage product of GPIb) did not activate platelets but inhibited aggregation of the platelets by von Willebrand factor and their activation by thrombin (see page 7, 1st col. 1st full ¶ and page 8, 2nd col., at the end of the 1st ¶ in particular). Further, Wicki et al teach that the platelets that platelets were washed with calcium-free Tyrode's buffer (see page 1, 2nd col. last ¶ in particular) which is considered to be a pharmaceutical acceptable carrier. Further Wicki et al teach that Fab fragments of rabbit IgG were prepared by digestion with papain followed by ion-exchange chromatograph on CM-cellulose and gel filtration on Ultrogel AcA 34 (see page 2, 2nd paragraph, 1st ¶ in particular). In order for the Fab fragments to be prepared on Ultrogel AcA 34 it must be eluted in a pharmaceutical acceptable carrier. Wicki et al conclude that Fab fragments from IgG of rabbit antibodies to the 45 kDa glycopeptide inhibit many of the platelet responses to thrombin including partial inhibition of shape-change (see page 9, 1st col., 2nd full ¶ in particular).

Given that the Fab fragments against GPIb inhibited aggregation of the the platelets by von Willebrand factor and their acivation by thrombin. Those skilled in the are would under stand this teachings to refer to the Fab as antithrombotic agent. Since the Fab frargments inhibit aggregation of the platelets then the Fab fragments do not incurr thrombocytopenia.

While the prior art teachings may be silent as to the "binds in vivo to human platelet glycoprotein GPIb without incurring thrombocytopenia" per se; the product used in the reference is the same as the claimed product. Therefore, the claimed "binds in vivo to human platelet glycoprotein GPIb without incurring thrombocytopenia" is considered inherent properties.

The Wicki et al reference teaches the same products and the intended uses do not carry patentable weight per se and the claims read on the active or essential ingredients of the Fab fragment against GPIb.

When a claim recites using an old composition or structure (e.g. Fab fragments against GPIb antibody) and the use is directed to a result or property of that composition or structure (binds in vivo to human platelet glycoprotein GPIb without incurring thrombocytopenia), then the claim is anticipated. See MPEP 2112.02. Also, see Bristol-Myers Squibb Co. v. Ben Venue

Laboratories, Inc. 58 USPQ2d 1508 (CA FC 2001); Ex parte Novitski 26 USPQ 1389 (BPAI 1993); Mehl/Biophile International Corp. V. Milgraum, 52 USPQ2d 1303 (Fed. Cir. 1999); Atlas Powder Co. V. IRECO, 51 USPQ2d 1943 (Fed. Cir. 1999).

The reference teachings anticipate the claimed invention.

9. Claims 80-82 are allowable

10. Claims 70-71are objected to as being dependent upon a rejected base claim, but would be allowable if rewritten in independent form including all of the limitations of the base claim and any intervening claims.

11. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Maher Haddad whose telephone number is (571) 272-0845. The examiner can normally be reached Monday through Friday from 7:30 am to 4:00 pm. A message may be left on the examiner's voice mail service. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Christina Chan can be reached on (571) 272-0841. The fax number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

August 23, 2006

Maher Haddad

Maher Haddad, Ph.D.
Primary Examiner
Technology Center 1600